T1130-01-04

# Expandable Single-Component Gastroretention Devices:
## Shape Optimization & Proof of Concept for Extended Gastric Residency and Drug Release *In Vivo*

Alexander Stahl, PhD; Manasi Chawathe Baker, PhD; Stephanie Reed, PhD
Secant Group, LLC, Telford, PA

CONTACT: alex.stahl@secant.com

## PURPOSE

Gastroretentive drug administration strategies prolong the release of an orally dosed active pharmaceutical ingredient (API) within the stomach, leading to greater patient convenience and compliance through the reduced need for redosing. Our group has developed an expandable gastroretentive platform based on the flexible, biocompatible, and biodegradable polymer Hydralese™ (poly(glycerol sebacate) urethane; PGSU). Even at high levels of API encapsulation (API content up to 60% of overall device mass), Hydralese (PGSU)-based constructs are highly elastic and can fold up to fit inside oral delivery capsules and spring back to their expanded form upon reaching the stomach. Once expanded, the device is too large to pass through the pyloric sphincter and remains in the stomach, releasing the API payload until eventual degradation and loss of mechanical integrity, which leads to device elimination.

## OBJECTIVES

In this study, our three main aims were (1) to demonstrate that a single-component Hydralese (PGSU)-based device can remain in the stomach for as long as one month, (2) to quantify the release kinetics of a model API-loaded gastroretentive device *in vivo*, and (3) to optimize device shape for packing into capsules and long-term residency in the stomach.

## METHODS

Device biocompatibility and functionality *in vivo* were investigated using porcine and canine models. Finite element analysis (FEA) was used to explore how changes to the device geometry affect mechanical performance.

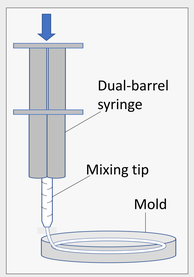
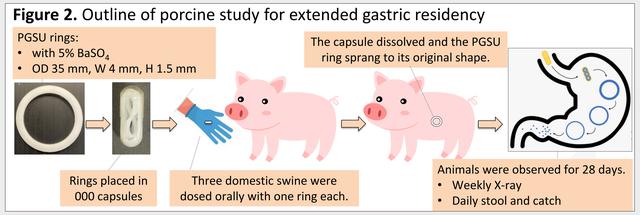



**Figure 1.** API-loaded Hydralese (PGSU) devices were fabricated by reaction injection molding. Prepolymer resin and API particles were loaded into a dual-barrel syringe. One barrel also contained hexamethylene diisocyanate as a crosslinking agent, the other barrel contained tin(II) 2-ethylhexanoate as a catalyst. Both sides were passed through a mixing tip and extruded into a mold. Curing occurred within a few minutes under ambient conditions.

## RESULTS

**Figure 2.** Outline of porcine study for extended gastric residency




- *Gross pathology revealed no notable or dramatic findings relating to device safety or tolerability.*
- *Two of the rings remained intact in the stomach for 28 days until the study's end.*
- *One ring passed intact at Day 19.*

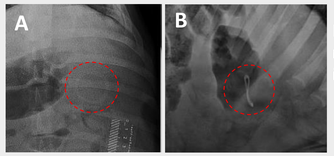



**Figure 3.** Radiographs showing a ring at **(A)** Day 0 and **(B)** Day 28 in the swine stomach.

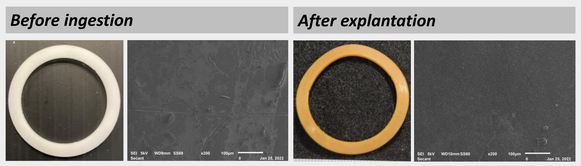
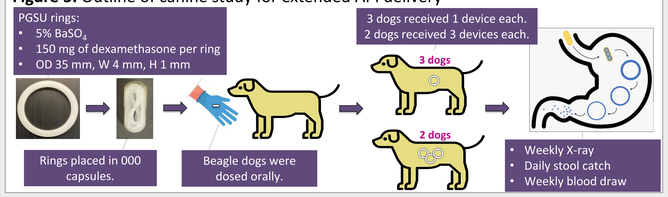



**Figure 4.** Images of a ring before and after 28 days in the porcine gastric environment. Some surface pitting was visible by scanning electron microscopy (SEM) post-explantation.

| Gastroretentive Device | Time *in vivo* (days) | Width loss (%) | Thickness loss (%) |
|---|---|---|---|
| Placebo rings (5% $BaSO_4$) 1.5x4x35 mm | 28 | 5.11 ± 2.36 | 6.71 ± 1.37 |

**Table 1.** Hydralese rings experienced small dimensional losses after 28 days in the porcine gastric environment.

**Figure 5.** Outline of canine study for extended API delivery



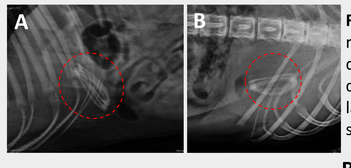




**Figure 6.** Radiographs showing three rings on **(A)** Day 0 and **(B)** Day 14 in the dog stomach. The three devices were dosed in separate capsules and aligned later, likely due to forces exerted by the stomach wall.

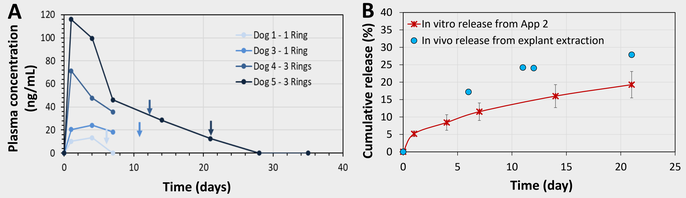



**Figure 7. (A)** Dexamethasone levels in the dog plasma. Arrows indicate the day that devices were eliminated. **(B)** Comparison of dexamethasone release from rings *in vitro* and *in vivo*. *In vivo* values were obtained by extracting the remaining API from devices post-elimination.

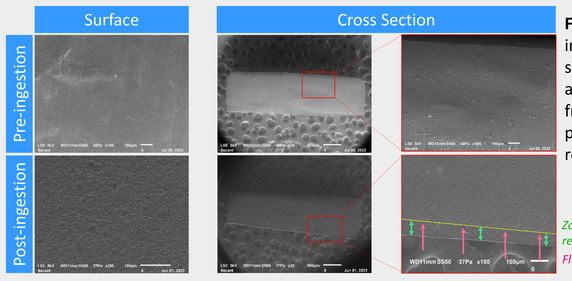



**Figure 8.** SEM images show surface pitting and API release front following period of gastric residency.

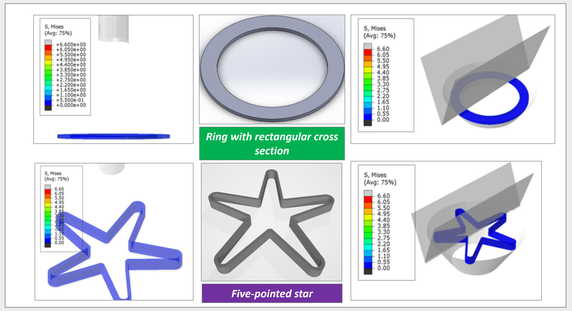



**Figure 9.** FEA was used to calculate stress concentrations and resistive forces for different device shapes as they are folded into a capsule and pushed through a sphincter-like opening.

## CONCLUSIONS

Successfully dosed PGSU devices in animal models

- PGSU material survived intact up to one month
- Drug release was sustained for duration of device residency in GI tract
- Rapid API clearance followed device elimination
- No adverse physiological responses observed
- Differences seen between porcine and canine models, with mean device gastric residence time longer in swine

FEA modelling of PGSU devices

- Predicted stresses observed during device folding
- Compared device resistance to passing through a sphincter-like opening
- Can inform future device design optimization

## ACKNOWLEDGEMENTS

Secant Group would like to thank our collaborators on this project, Charles River (execution of *in vivo* studies) and Fidelis (FEA modeling).

## REFERENCES

1. Reed, S., Stahl, A., Baker, M.C., Gabriele, P., Weber, A. "Shape-guided controlled release and retention with structures including crosslinked poly(glycerol sebacate)" (2020), *Patent Application No. 17/365,139.*
2. Reed, S., Smoot, C., Shull, D., Crumbling, T., D'Ottavio, J., Gabriele, P. D., Ely, J. "Tunable, controlled-release, urethane-containing elastomers and processes of forming the same" (2020). *U.S. Patent Application No. 16/547,175*.
3. Nicholson, C. B., Harris, J. J., Gabriele, P. D. "Water-mediated preparations of polymeric materials" (2016). *U.S. Patent No. 9,359,472*.
4. https://secant.com/business/resorbable-polymers-for-controlled-release

secant group
PARTNERS FROM INSPIRATION TO REALIZATION